

PATENT  
Attorney Docket No.: ANGL-06602

## REMARKS

### I. Claims 1-15 and 18-27 Are Enabled

The Examiner has rejected Claims 1-15 and 18-27 under 35 U.S.C. § 112, first paragraph, on the grounds that "the recitation of 'oral fluid' in the amended claim 1 is not provided in the specification." The Examiner states that, "[a]lthough saliva is considered oral fluid, blood, phlem and pus is oral fluid is well and support in the specification only provides for saliva." Office Action, page 2. Applicants respectfully disagree, and submit that the claims are fully enabled within the specification. Nevertheless, for the purpose of furthering prosecution of the present application, without acquiescing to the Examiner's arguments, and without waiving the right to prosecute the amended claims (or similar claims) in the future, Applicants have amended the language of Claim 1 to replace the term "oral fluid" with "saliva." Applicants note that saliva typically contains components of blood, pus, and other components secreted by various glands (*e.g.*, endocrine glands). The presently claimed invention functions with a range of such saliva components.

### II. Claims 1-4 and 11 Are Not Anticipated

The Examiner has rejected Claims 1-4 and 11 under 35 U.S.C. § 102 as allegedly being anticipated by Manautou *et al.* (U.S. Patent No. 3,875,013). Office Action, page 3. The Federal Circuit has stated the relevant analysis for anticipation as follows: "A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Applicants respectfully submit that the reference cited by the Examiner does not teach each element of the Claims.

Specifically, the Manautou *et al.* reference contains no teaching of the use of a non-toxic chromogen, which is a novel and essential element of the presently claimed invention. Rather, Manautou *et al.* teaches the use of p-nitrophenol, a compound known for its toxicity. In support of this, Applicants submit herewith as Exhibit A a data sheet from NTP Chemical Repository describing the properties of p-nitrophenol. In particular, Applicants note the following characteristics related to ingestion of, or skin contact with, p-nitrophenol: "This compound is highly toxic by ingestion, inhalation or absorption through the skin. When heated to

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decomposition it emits toxic fumes. It is corrosive to the skin . . . Phenols are very toxic poisons AND corrosive and irritating, so that inducing vomiting may make medical problems worse." NTP Chemical Repository Data Sheet printout, pages 3-5.

The Examiner has argued that "Manautou et al teaches the use of an oral test strip that comprise [sic] of p-nitrophenol that is apparently safe to use orally." Office Action, page 7. This assertion appears to be based on the fact that the Manautou patent makes prophetic reference to oral use of test strips comprising p-nitrophenol. However, the Examiner has not cited, and cannot cite, evidence that p-nitrophenol-based test strips have been found safe for practical use, or have found such use in the real-world marketplace (i.e., the Manautou patent is suggesting use of a toxic compound—there is no evidence in the record showing the lack of toxicity in Manautou's product. Patents can be filed with unuseful or unsafe inventions. The fact that Manautou's chemistry is disclosed in a patent does not mean that it is non-toxic). Applicants have cited substantial evidence, on the other hand, of p-nitrophenol's high toxicity, and consequent unsuitability for oral use of the type contemplated by the presently claimed invention. Moreover, the non-toxic chemistry of the present invention is in widespread public use, and has met with great commercial success. Because Manautou et al. fails to teach the use of a non-toxic chromogen, it consequently fails to teach each element of the claims of the present invention. Accordingly, Applicants respectfully submit that Claims 1-4 and 11 are not anticipated by Manautou et al., and request that the rejection be withdrawn.

### III. Claims 5-15 and 18-27 Are Nonobvious

#### A. The Claims Are Not Unpatentable Over Manautou et al. in View of Bogema

The Examiner has rejected Claims 5-6, 8-15, and 18-27 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Manautou et al. in view of Bogema (U.S. Patent No. 6,248,598). Office Action, page 3. Applicants respectfully disagree. Under § 2143 of the Manual of Patent Examining Procedure (M.P.E.P), there are three criteria that must be met to provide a *prima facie* showing of obviousness. The first is that the prior art must teach or suggest all of the claim limitations. The second is a suggestion or motivation in the references or the knowledge generally available to combine the reference teachings. The third is a reasonable expectation of success should the combination be carried out. Failure to establish even one of these requirements means that the Examiner has failed to establish a *prima facie* case

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of obviousness. Applicants respectfully submit that the Examiner has failed to set forth a *prima facie* case of obviousness because these requirements have not been met.

As explained above, and as evidenced by the toxicity data provided in the attached NTP Chemical Repository Data Sheet, Manautou et al. contains no teaching of a non-toxic chromogen for oral testing. Indeed, none of the prior art cited by the Examiner, including the Bogema reference, teaches the use of a non-toxic chromogen for oral testing. Thus, there is no teaching of all of the claim limitations of the presently claimed invention in the cited art, alone or in combination. As such, there can also be no reasonable expectation of success in combining the cited references to achieve the presently claimed invention, since an essential element is absent. Moreover, the wholesale lack of a teaching of the use of a non-toxic chromogen for oral testing in the prior art is further evidence of the nonobvious nature of the presently claimed invention. Applicants respectfully submit that, because there is no teaching of the use of a non-toxic chromogen, the Examiner has failed to set forth a *prima facie* showing of obviousness under M.P.E.P. § 2143. Applicants thus respectfully request that the rejection be withdrawn.

**B. The Claims Are Not Unpatentable Over Manautou et al. in View of Kindler**

The Examiner has rejected Claim 7 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Manautou et al. in view of Kindler (U.S. Patent No. 5,494,831). Office Action, page 5. Applicants respectfully disagree, and submit that the Examiner has failed to set forth a *prima facie* showing of obviousness as required under M.P.E.P. § 2143.

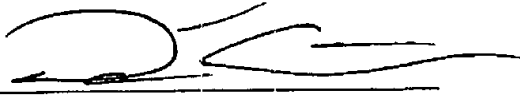
As discussed above, none of the prior art cited by the Examiner, including both the Manautou et al. and Kindler references, teaches the use of a non-toxic chromogen for oral testing. Thus, there is no teaching of all of the claim limitations of the presently claimed invention in the cited art, alone or in combination. As such, there can also be no reasonable expectation of success in combining the cited references to achieve the presently claimed invention, since an essential element is absent. As stated above, the absence of a teaching of the use of a non-toxic chromogen for oral testing in the prior art is further evidence of the nonobvious nature of the presently claimed invention. Applicants respectfully submit that, because there is no teaching of the use of a non-toxic chromogen, the Examiner has failed to set forth a *prima facie* showing of obviousness under M.P.E.P. § 2143. Applicants thus respectfully request that the rejection be withdrawn.

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### CONCLUSION

All grounds of rejection of the Office Action mailed June 3, 2003 have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that Applicants' claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

Dated: 9/3/03

  
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**EXHIBIT A:**

NTP Chemical Repository Data Sheet for p-nitrophenol

H&amp;S:P-NITROPHENOL 100-02-7

[http://ntp-support.niehs.nih.gov/NTP\\_Re...m\\_HS\\_HTML/NTP\\_Chem1/Radian100-02-7.html](http://ntp-support.niehs.nih.gov/NTP_Re...m_HS_HTML/NTP_Chem1/Radian100-02-7.html)NTP CHEMICAL REPOSITORY  
P-NITROPHENOL-IDENTIFIERS  
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\*CATALOG ID NUMBER: 000049

\*CAS NUMBER: 100-02-7

\*BASE CHEMICAL NAME: NITROPHENOL, P-

\*PRIMARY NAME: P-NITROPHENOL

\*CHEMICAL FORMULA: C6H5NO3

\*STRUCTURAL FORMULA: OHC6H5NO2

\*WLN: WNR DQ

## \*SYNONYMS:

4-HYDROXYNITROBENZENE  
P-NITRO-PHENOL  
4-NITROPHENOL  
NCI-C55992  
PNP  
PARA-NITROPHENOL  
PHENOL, P-NITRO-  
UN 1663  
PHENOL, 4-NITRO  
NIPHEN  
P-HYDROXYNITROBENZENE  
MONONITROPHENOL-PHYSICAL CHEMICAL DATA  
=====\*PHYSICAL DESCRIPTIONS: LITERATURE: Colorless to slightly yellow crystals  
REPOSITORY: Beige solid

\*MOLECULAR WEIGHT: 139.11

\*SPECIFIC GRAVITY: 1.270 @ 20/4 C

\*DENSITY: 1.479-1.495 g/mL @ 20 C

\*MP (DEG C): 113-115 C (Sublimes)

\*BP (DEG C): 279 C (Decomposes)

## \*SOLUBILITIES:

WATER : &lt;0.1 mg/mL @ 21 C (RAD)

DMSO : &gt;=100 mg/mL @ 21 C (RAD)

95% ETHANOL : &gt;=100 mg/mL @ 21 C (RAD)

METHANOL : Not available

ACETONE : &gt;=100 mg/mL @ 21 C (RAD)

TOLUENE : Soluble

## OTHER SOLVENTS:

Carbon disulfide: Slightly soluble  
Pyrimidine: Soluble  
Chloroform: Very soluble  
Fixed alkali hydroxides: Soluble  
Carbonates: Soluble  
Ether: Very soluble  
Benzene: Soluble in hot; slightly soluble in cold

## \*VOLATILITY:

Vapor pressure: 1 mm Hg @ 20 C; 18.7 mm Hg @ 186 C; 2.2 mm Hg @ 146 C  
Vapor density : 1.244 @ 65 C

## \*FLAMMABILITY (FLASH POINT):

The flash point for this chemical is 192 C (377 F). It is combustible.  
Fires involving this compound should be controlled using a dry chemical,  
carbon dioxide or Halon extinguisher.

\*UEL: Not available

LEL: Not available

## \*REACTIVITY:

This compound is incompatible with oxidizing agents, organics, combustible  
substances and reducing agents.

## \*STABILITY:

This compound is stable under normal laboratory conditions. Solutions of this  
chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours  
under normal lab conditions (RAD).

## \*OTHER PHYSICAL DATA:

Odorless  
Sweet then burning taste  
Freezing point: 113 C  
Slightly volatile with steam

## -TOXICITY

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\*NIOSH REGISTRY NUMBER: SM2275000

## \*TOXICITY: (abbreviations)

typ.	dose	mode	specie	amount	unit	other
	LD50	orl	rat	250	mg/kg	
	LDLo	scu	rat	200	mg/kg	
	LD50	orl	mus	380	mg/kg	
	LD50	ipr	mus	75	mg/kg	
	LDLo	ivn	dog	10	mg/kg	
	LD50	unr	cat	150	mg/kg	
	LDLo	scu	gpg	200	mg/kg	
	LDLo	ims	pgn	65	mg/kg	
	LDLo	scu	frg	60	mg/kg	
	LD50	orl	mam	247	mg/kg	
	LD50	skn	mam	920	mg/kg	

\*AQTX/TLM96: Not available

## \*SAX TOXICITY EVALUATION:

TER = HIGH via oral, subcutaneous, intraperitoneal, intravenous and intramus-  
cular routes.

## \*CARCINOGENICITY:

Status: NTP Carcinogenesis Studies; on test, November 1985

## \*MUTATION DATA:

H&amp;S:P-NITROPHENOL 100-02-7

[http://ntp-support.niehs.nih.gov/NTP\\_Re...m\\_HS\\_HTML/NTP\\_Chem1/Radian100-02-7.html](http://ntp-support.niehs.nih.gov/NTP_Re...m_HS_HTML/NTP_Chem1/Radian100-02-7.html)

test	lowest dose	test	lowest dose
-----	-----	-----	-----
dnd-esc	50 umol/L	dnr-omi	10 mg/plate
mrc-smc	21 mmol/L	dni-hmn:fbr	1 mmol/L

\*TERATOGENICITY (Reproductive Effects Data): Not available

\*STANDARDS, REGULATIONS & RECOMMENDATIONS:

OSHA: None  
ACGIH: None  
NIOSH Criteria Document: None  
NFPA Hazard Rating: Health (H): None  
Flammability (F): None  
Reactivity (R): None

\*OTHER TOXICITY DATA:

Review: Toxicology Review  
Standards and Regulations: DOT-IMO: Poison B; Label: St. Andrews Cross  
Status: Reported in EPA TSCA Inventory, 1983  
EPA Genetic Toxicology Program, January 1984  
Meets criteria for proposed OSHA Medical Records Rule

-OTHER DATA (Regulatory)

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\*PROPER SHIPPING NAME (IATA): Nitrophenols

\*UN/ID NUMBER: UN1663

\*HAZARD CLASS: 6.1                      SUBSIDIARY RISK: None                      PACKING GROUP: III

\*LABELS REQUIRED: Keep away from food

\*PACKAGING: PASSENGER: PKG. INSTR.: 619, Y619                      MAXIMUM QUANTITY: 100 kg, 10 kg  
CARGO : PKG. INSTR.: 619                      MAXIMUM QUANTITY: 200 kg

\*SPECIAL PROVISIONS: None

\*USES:

Indicator in 0.1% alcohol solution, intermediate in organic synthesis, production of parathion, fungicide for leather, indicator in water analysis, bactericide.

\*COMMENTS:

Reviewed by: RLT/860626

-HANDLING PROCEDURES

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\*ACUTE/CHRONIC HAZARDS:

This compound is highly toxic by ingestion, inhalation or absorption through the skin. When heated to decomposition it emits toxic fumes. It is corrosive to the skin.

\*MINIMUM PROTECTIVE CLOTHING:

If Tyvek-type disposable protective clothing is not worn during handling of this chemical, wear disposable Tyvek-type sleeves taped to your gloves.

\*RECOMMENDED GLOVE MATERIALS:

Recommended Glove Type For Use With Neat (Undiluted) Chemical:  
Recommendations based on permeation test results are made for handling the neat (undiluted) chemical. If this chemical makes direct contact with



your glove, or if a tear, puncture or hole develops, replace them at once.

Suggested Glove Type(s) (RAD): No information available

**\*RECOMMENDED RESPIRATOR:**

Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO<sub>2</sub>) with a dust/mist filter.

**\*OTHER:** Not available

**\*STORAGE PRECAUTIONS:**

You should store this chemical under refrigerated temperatures, and keep it away from oxidizing materials. STORE AWAY FROM SOURCES OF IGNITION.

**\*SPILLS AND LEAKAGE:**

Should a spill occur while you are handling this chemical, FIRST REMOVE ALL SOURCES OF IGNITION, then you should dampen the solid spill material with 60-70% ethanol and transfer the dampened material to a suitable container. Use absorbent paper dampened with 60-70% ethanol to pick up any remaining material. Seal the absorbent paper, and any of your clothes, which may be contaminated, in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with 60-70% ethanol followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

**\*DISPOSAL AND WASTE TREATMENT:**

You should dispose of all waste and contaminated materials associated with this chemical as specified by existing local, state and federal regulations concerning hazardous waste disposal. It is suggested that your contaminated materials should be destroyed by incineration in a special, high temperature (>2000 degrees F), chemical incinerator facility.

**-EMERGENCY PROCEDURES**

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**\*SKIN CONTACT:**

IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.

IMMEDIATELY call a hospital or poison control center even if no symptoms (such as redness or irritation) develop.

IMMEDIATELY transport the victim to a hospital for treatment after washing the affected areas.

**\*INHALATION:**

IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.

Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

**\*EYE CONTACT:**

First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.

Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.

IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

**\*INGESTION:**

DO NOT INDUCE VOMITING. Phenols are very toxic poisons AND corrosive and irritating, so that inducing vomiting may make medical problems worse. IMMEDIATELY call a hospital or poison control center and locate activated charcoal, egg whites, or milk in case the medical advisor recommends administering one of them.

If advice from a physician is not readily available and the victim is conscious and not convulsing, give the victim a glass of activated charcoal slurry in water or, if this is not available, a glass of milk, or beaten egg whites and IMMEDIATELY transport victim to a hospital.

If the victim is convulsing or unconscious, do not give anything by mouth, assure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

**\*SYMPTOMS:**

Symptoms following exposure to this compound may include irritation of the skin, eyes, nose and throat, headache, loss of consciousness, drowsiness, nausea, cyanosis, liver and kidney damage, methemoglobinemia, central nervous system depression, dyspnea, sweating, dry throat, fever, muscular weakness, fatigue, irritability, abdominal cramps, dermatitis, corneal damage and hypothermia.

**-SOURCES**

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**\*SOURCES:**

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H&amp;S:P-NITROPHENOL 100-02-7

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Last revised: 13 August 2001

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